

### **REMARKS**

This responds to the Office Action mailed on April 15, 2010.

Claims 1, 3, 4, 7, and 10 are amended. Claim 9 is canceled. Claims 1-7 and 10 are pending.

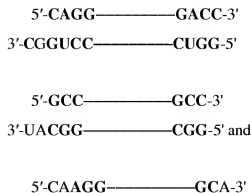
Claims 9-10 were not rejected. Therefore, pending claim 10 is assumed to be allowable.

Claims 1-7 were rejected under 35 U.S.C. § 112, first paragraph, and under 35 U.S.C. § 112, second paragraph. The amendment to claim 1 to delete “that are complementary” renders these rejections moot.

Claims 1-7 were rejected under 35 U.S.C. § 103(a) as being obvious over Kreutzer et al. (U.S. Publication No. 2004/0001811), Elbashir et al. (Methods, 26:199 (2002)), Nilsen et al. (U.S. Patent No. 6,013,447), De Young et al. (Biochemistry, 33:12127 1994)), Hernandez (EMBO, 4:1827 (1985)), and Skuzeski et al. (J. Biol. Chem., 259: 8345 (1984)). This rejection, as it may be maintained with respect to the pending claims, is respectfully traversed.

Kreutzer et al. disclose a double stranded (ds) RNA with a RNA strand having a region that is less than 25 nucleotides in length and complementary to at least a portion of a RNA transcript of an anti-apoptotic gene such as Bcl-2. Kreutzer et al. also disclose that the individual strands of a dsRNA can be expressed from two separate vectors or from the same vector, or as an inverted repeat joined by a linker polynucleotide so as to form a stem and loop structure, and that the promoter can be a PolI promoter, PolII promoter, PolIII promoter or a prokaryotic promoter. However, the ssRNAs used to prepare dsRNAs for transfection in the Examples were prepared by conventional oligonucleotide chemical syntheses.

The dsRNAs in the Example in Kreutzer et al. have the following ends:



3'-UCUGUCC—————CG-5'.

Elbashir et al. disclose the use of small interfering RNAs (siRNAs; 21 to 23 nucleotides in length), which are the products of RNase III digestion of dsRNAs formed with mRNA, to silence genes in mammalian cells. It is disclosed that the predominant siRNAs formed in cells are 21 and 22 nucleotide RNAs with symmetric 2 nucleotide 3' overhangs (see Figure 4B which shows "TT" overhangs). Elbashir et al. disclose that 21 nucleotide RNAs useful to form siRNAs are prepared via conventional oligonucleotide chemical syntheses and annealed prior to transfection.

The products disclosed in Kreutzer et al. and Elbashir et al. have two 5' ends and two 3' ends in contrast to the products produced by Applicant's vectors. Moreover, neither Kreutzer et al. nor Elbashir et al. provide vectors for expressing siRNAs or miRNAs.

Nilsen et al. relate to vectors and methods to identify effector RNA molecules that inhibit expression of target RNA molecules (abstract). No sequences identified by the method are described.

De Young et al. disclose the use of vectors with a U1 snRNA promoter and U1 snRNA terminator sequence, and a T7 promoter and T7 terminator sequence, to express ANF-specific ribozymes. Ribozymes, in contrast to siRNA and miRNA, are catalytic and so only a small amount of a ribozyme can yield a detectable effect. In contrast, siRNA or miRNA is not catalytic and so larger amounts of those molecules are needed to result in a detectable effect.

Hernandez discloses a vector to detect the processing of U1 nuclear RNA, which is transcribed by PolII and is involved in mRNA splicing. The vector includes an internally deleted U1 gene expressed from the SV40 promoter/enhancer. The vector was introduced to cells and the resulting RNA analyzed. The results showed that the first U1 RNA precursor has a few extra nucleotides at the 3' end which are shortened to form mature U1 RNA, and that a 13 nucleotide sequence 3' of the coding region is required to direct the first step in the formation of the 3' end of U1 snRNA.

Skuzeski et al. disclose the identification of two regions at the U1 promoter essential for transcription of human U1 RNA and that there is a *Bgl*III site immediately 5' to the U1 coding region (Figure 5).

None of Kreutzer et al., Elbashir et al., Nilsen et al., De Youngs et al., Hernandez or Skuzesli et al. provides a reasonable expectation that expression of disclosed sequences from the U1 promoter/terminator in a vector would yield products that form a stem loop structure and result in siRNA or miRNA in a cell.

The Examiner asserts that none of the advantages of the claimed expression vector as argued in the Amendment filed on February 23, 2010, are recited in the claims.

Applicant respectfully disagrees. The claims recite that the recombinant vector provides for the correct, stable and effective expression in mammalian cells of a siRNA or a miRNA. Moreover, claims 1, 3 and 10 as amended recite that the nucleotide(s) at the 3' end are selected to allow for asymmetry in siRNA strand selection into an interference complex, which is disclosed as decreasing the accumulation of the sense strand into complexes which in turn decreases undesired targeting. Further, the presence of a short stem in an expressed product of Applicant's vector, created by AUAC at the 5' end and UUUA at the 3' end (see claims 4 and 10), shows enhanced processing and release of the pre-siRNA or pre-miRNA.

Accordingly, withdrawal of the § 103 rejection is respectfully requested.

**CONCLUSION**

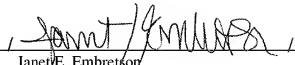
Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's representative at (612) 373-6959 to facilitate prosecution of this application.

If necessary, please charge any additional fees or deficiencies, or credit any overpayments to Deposit Account No. 19-0743.

Respectfully submitted,

SCHWEGMAN, LUNDBERG & WOESSNER, P.A.  
P.O. Box 2938  
Minneapolis, MN 55402--0938  
(612) 373-6959

Date August 16, 2010

By   
Janet E. Embretson  
Reg. No. 39,665

**CERTIFICATE UNDER 37 CFR 1.8:** The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 16th day of August, 2010.

  
CHERYL L. KNAPP